

### III. REMARKS

Claims 26-45 of United States Serial No. 10/520,239 are pending. Upon entry of this amendment, claims 26-34, and 36-44 will remain pending in this application. Applicants respectfully request favorable reconsideration and allowance of the claims.

#### 35 U.S.C. §112

Claims 26-45 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking certain enablement for the reasons set forth in the Office Action at pages 5-11.

Claims 26-45 have also been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as their invention for the reasons set forth in the Office Action at pages 2-4.

The Office Action states that redefinition of Y-L-Y' to be derived from beta-dicarbonyl compounds would overcome the above-referenced 35 U.S.C. §112 rejections. Applicants have amended their claims in the manner helpfully suggested by the Examiner. The independent claims have been further amended to recite the ligands of originally claimed formulas (II) and (XII), wherein moieties T, T', T'', and T''' comprise oxygen. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. §112 first and second paragraph rejections of claims 26-45.

**35 U.S.C §102**

Claims 26-45 have been rejected under 35 U.S.C. §102(b) as being anticipated by Kuhlwein et al. ("Kuhlwein"), Kramer et al. ("Kramer"), Everaere et al. ("Everaere"), and Carmona et al. ("Carmona").

In the Patent Act of 1952, Section 100(b) defined "process" as follows: "The term 'process' means process, art or method, and *includes a new use of a* known process, machine, manufacture, *composition of matter*, or material." (Emphasis added.) In Perricone v. Medicus Pharmaceutical Corp., 432 F.3d 1368, 77 U.S.P.Q.2d 1321 (Fed. Cir. 2005), the United States Court of Appeals for the Federal Circuit held that new uses of old products or processes are indeed patentable subject matter. See 35 U.S.C. § 101 (2000) (identifying as patentable 'any new and useful improvements' of a process, machine, manufacture, etc.). The Federal Circuit also explained in Catalina Marketing International, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 809 (Fed. Cir. 2002) that a patent to an apparatus does not necessarily prevent a subsequent inventor from obtaining a patent on a new method of using the apparatus. See also In re King, 801 F.2d 1324, 1326 (Fed. Cir. 1986) (principles of inherency do not prohibit a process patent for a new use of an old structure).

MPEP § 2131 mandates that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegall Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987)." MPEP at 2100-67. Claims 27-45 depend ultimately from claim 26, and therefore contain the respective elements or features of claim 26 neither disclosed in Kuhlwein, Kramer, Everaere nor Carmona.

The present claims are directed to a method of treating cancer by administering a therapeutically effective amount of the claimed Ruthenium compound to a subject in need thereof. Although the references cited in the Office Action all disclose the synthesis of Ruthenium-containing compounds, none of Kuhlwein, Kramer, Everaere or Carmona disclose or suggest using a Ruthenium compound in a method of treating cancer as presently claimed by Applicants. Kuhlwein disclose transition metal complexes of curcumin and derivatives. See Abstract, p. 1211. Kramer disclose metal-promoted peptide synthesis from amino acid esters. See Introduction, p. 1518. Everaere disclose a series of  $\beta$ -amino alcohol ligands for the transfer hydrogenation of a variety of functionalized ketones. See Introduction, p. 275. Carmona disclose the structures of *p*-cymeneruthenium(II) complexes containing hydroxypyrazole and indazole ligands. See Introduction, p. 1463. Applicants respectfully submit that Kuhlwein, Kramer, Everaere and Carmona do not disclose a method of treating cancer which comprises administering to a subject in need of treatment a therapeutically effective amount of a ruthenium(II) compound of claimed formula (I).

The determination of whether a preamble limits a claim is made on a case-by-case basis in light of the facts in each case; there is no litmus test defining when a preamble limits the scope of a claim. Catalina Mktg. Int'l v. Coolsavings.com, Inc., 289 F.3d 801, 808, 62 USPQ2d 1781, 1785 (Fed. Cir. 2002). "[A] claim preamble has the import that the claim as a whole suggests for it." Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995). "If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is 'necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim." Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999). See also Jansen v. Rexall Sundown, Inc., 342 F.3d 1329, 1333, 68 USPQ2d 1154, 1158 (Fed. Cir. 2003) (In considering the effect of the preamble in a claim directed to a method of treating or preventing pernicious anemia in humans by administering a certain vitamin

preparation to "a human in need thereof," the court held that the claims' recitation of a patient or a human "in need" gives life and meaning to the preamble's statement of purpose.)

The preambles of independent claims 26 and 36 recite "[a] method of treating cancer" and "[a] method of treating ovarian adenocarcinoma" respectively. The phrases "a method of treating cancer" and "a method of treating ovarian adenocarcinoma" found in the preambles give meaning to the claims, as they further define the scope of the claimed processes. It is only by those phrases that it can be known that the subject matter defined by the claims is comprised as a method of treating cancer and a method of treating ovarian adenocarcinoma. Consequently, the claim preambles cannot be ignored. While Kuhlwein, Kramer, Everaere and Carmona teach Ruthenium compounds, there is no disclosure or teaching that the Ruthenium compounds are utilized in a method of treating cancer. As each and every limitation of claims of the present application is not disclosed by Kuhlwein, Kramer, Everaere or Carmona, claims 26 and 36 are not anticipated by the aforementioned references. Claims 27-35 depend from independent claim 26, and claims 37-45 depend from independent claim 36. Therefore, dependent claims 27-35, and 37-45 are also not anticipated by Kuhlwein, Kramer, Everaere and Carmona. Applicants therefore respectfully request withdrawal of the 35 U.S.C. §102(b) rejection.

Furthermore, Kramer and Everaere do not anticipate the claimed Ruthenium compound structure. Kramer and Everaere disclose structures that complex the Ruthenium metal atom via nitrogen and oxygen atoms. By contrast, the claimed compound complexes the Ruthenium metal atom via two carbonyl atoms.

**35 U.S.C §103**

Claims 26-45 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Morris et al. (WO 2001030790) in view of Kuhlwein, Kramer, Everaere and Carmona. It is expressly conceded in the Office Action that Morris et al. do not explicitly teach the claimed cyclic Ru complexes in which the bidentate ligand is negatively charged. However, the Office Action alleges that one of ordinary skill in the art at the time the invention was made would have been aware of Ru complexes containing negatively charged bidentate ligands and would have been motivated to test all available Ru complexes in searching for additional derivatives of Ru complexes taught by Morris et al., and would therefore have arrived at the claimed compounds with reasonable expectation of success.

Given the considerable difference in chemical structure between the ligands in Morris et al. and those in Kuhlwein, Kramer, Everaere and Carmona, Applicants respectfully traverse the rejection. In particular, the ligands in Morris are neutral and complex to the Ru metal atom via nitrogen atoms, which is in stark contrast to the negatively charged ligands of the presently claimed method which complex the Ru metal atom via carbonyl oxygen atoms.

The present Office Action appears to present an "obvious to try" rationale, in suggesting that it would be obvious to try all available Ru complexes in searching for additional derivatives of Ru complexes taught by Morris and arrive at the instantly claimed compounds with a reasonable expectation of success. The "obvious to try" rationale requires, *inter alia*, a finding that at the time of the invention, there was a recognized problem or need in the art; that there be a finite number of identified, predictable potential solutions to a recognized need or problem; and that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success. MPEP 2143. Applicants assert that none of these requirements are met for the present claims.

In regard to the first finding required for the "obvious to try" rationale (that there was a recognized problem or need in the art at the time of invention), page 14, first paragraph of the Office Action merely alleges that the claims would have been obvious because obviousness based on similarity of structure and functions entails motivation to make the claimed compounds in expectation that compounds of similar structure will have similar properties. This allegation, however, fails to identify the specific problem or need in the art that would have motivated one of ordinary skill to pursue any alleged compounds of similar structure or properties.

The Office Action also fails to allege that there was some teaching, suggestion, or motivation which would have led one of ordinary skill to modify the compounds of the cited references to arrive at the instant claims. In Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1356-1357 (Fed. Cir. 2007), decided after *KSR*, the Federal Circuit stated the following, "[The] test for prima facie obviousness for chemical compounds is consistent with the legal principles enunciated in *KSR* ... **Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.** In Takeda Chemical Industries, Alphapharm argued that it was obvious to select "compound b" and modify it by making "two obvious chemical changes: first, homologation, i.e., replacing the methyl group with an ethyl group, which would have resulted in a 6-ethyl compound; and second, 'ring-walking,' or moving the ethyl substituent to another position on the ring, the 5-position, thereby leading to the discovery of pioglitazone." *Id.* at 1357. The Federal Circuit, however, in affirming the district court, found that compound b was one of hundreds of millions of compounds disclosed in the art and that "[T]he prior art did not suggest to one of ordinary skill in the art that compound b would be the best candidate as the lead compound for antidiabetic research." *Id.* at 1358.

"The KSR Court recognized that '[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.' KSR, 127 S.Ct. at 1732. In such circumstances, 'the fact that a combination was obvious to try might show that it was obvious under §103.' *Id.* That is not the case here. Rather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation. Significantly, the closest prior art compound (compound b, the 6-methyl) exhibited negative properties that would have directed one of ordinary skill in the art away from that compound. Thus, this case fails to present the type of situation contemplated by the Court when it stated that an invention may be deemed obvious if it was 'obvious to try.' The evidence showed that it was not obvious to try."

*Id.* at 1359 (emphasis added).

Like Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd., the present Office Action suggests to modify Ru complexes containing neutrally charged ligands in order to arrive at the negatively charged ligands of the presently claimed method, which complex the Ru atom by means of oxygen. However, myriads of compounds disclosed in the art must be considered before one of ordinary skill would be led to select compounds of the Kuhlwein, Kramer, Everaere or Carmona references to modify Morris. Also like Takeda Chemical Industries, the teachings of Morris et al. are strictly limited to the Ru complexes having a neutral charge and Morris et al. fail to suggest why negatively charged ligands which complex the Ru atom via oxygen would be candidates in the treatment of cancer. Furthermore, neither of the Kuhlwein, Kramer, Everaere or Carmona references provides any teaching, suggestion or motivation for using any of their disclosed compounds in a method of treating cancer. Rather, Kuhlwein simply discusses transition metal complexes of curcumin and derivatives. Kramer only addresses metal-promoted peptide synthesis from amino acid esters. Everaere deals with a series of  $\beta$ -amino alcohol ligands for the transfer hydrogenation of a variety of functionalized ketones. Carmona merely focuses on synthesis of *p*-cymeneruthenium(II) complexes containing hydroxypyrazole and

indazole ligands. Therefore, as was the case in Takeda Chemical Industries, it is respectfully submitted that the Office Action fails to identify a reason why a chemist would be motivated to test all available Ru complexes in searching for additional derivatives of Ru complexes taught by Morris to arrive at the instantly claimed compounds with a reasonable expectation of success.

Morris et al. provide no teaching or suggestion whatsoever to one having ordinary skill in the art to support an expectation that an Ru compound having negatively charged ligands, wherein the ligand complexes with the Ru atom via carbonyl oxygen atoms, would have the same have similar properties or would function similarly in a biological system as an Ru compound having a neutrally charged ligand.

"Prior art did not render obvious a patent claiming a lead compound used in pharmaceutical approved for the treatment of duodenal ulcers, heartburn, and associated disorders, where compounds claimed by prior art differed structurally from compound claimed by patent, and the record contained no reasons a skilled artisan would have considered the differences between the compound identifiable and predictable." Eisai Co Ltd. V. Dr. Reddy's Laboratories, Ltd., 533 F.3d 1353, 87 USPQ.2d 1452 (Fed. Cr. 2008). The claimed compound in Eisai was rabeprazole and the prior art compounds were lansoprazole and omeprazole. The ONLY structural difference between the claimed rabeprazole and the prior art lansoprazole compounds is at the 4-position on the pyridine ring. Lansoprazol has a trifluoroethoxy (OCH<sub>2</sub>CF<sub>3</sub>) substituent, while rabeprazole as a methoxypropoxy (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>) substituent at the 4-position on the pyridine ring. The ONLY differences between the chemical structure of rabeprazole and omeprazole is that the pyridine ring of omeprazole is symmetrically substituted and has methoxy (OCH<sub>3</sub>) at the 4-position. All of these three compounds fall under the class of Brandstrom-disclosed structures, which comprise a benzimidazole bonded to a pyridine ring via a sulfinylmethyl group.



“To the extent that an art is unpredictable, as the chemical arts often are, KSR’s focus on these ‘identified, predictable solutions’ may present a difficult hurdle because potential solutions are less likely to be genuinely predictable”. Eisai Co Ltd. V. Dr. Reddy’s Laboratories, Ltd., 533 F.3d at 1359. “Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish a prima facie case of obviousness of a new claimed compound”. Eisai Co Ltd. V. Dr. Reddy’s Laboratories, Ltd., 533 F.3d at 1359, quoting Takeda, 492 F.3d at 1357. The present Office Action merely conjectures that one in the medicinal arts would be motivated try to modify any and all known Ru compounds to arrive at the presently claimed Ru compounds. This is merely a conclusion and does not constitute reasons why one having skill in the art would modify the Morris et al compounds. There are no specific reasons given why one having ordinary skill in the art would set out to test any and all Ru compounds, why the Morris Ru compounds would be modified to the presently claimed Ru compounds, or why there would be a reasonable expectation that Morris compounds and the presently claimed Ru compounds would have similar properties or functions in a biological system. The Office Action merely recites conclusions and, without more, is insufficient to establish a prima facie case of obviousness.

Additionally, there is no presumption of obviousness for homologous chemical compounds where there is no usefulness disclosed for the prior art compounds. In re Stemanski, 444 F.2d at 587, 170 USPQ at 348. In the present case, the four non-patent prior art journal articles appear to be papers relating to the synthesis of certain Ru compounds. There is no teaching or suggestion in any of these references to use Ru compounds in a method of treating cancer. Therefore, following Stemanski, the absence of a teaching of usefulness of the prior art compounds precludes a finding of obviousness.

In another relevant case, Applicant Langer filed a patent application directed to using sterically hindered amines as a dyeing agent in a catalytic polymerization process. The prior disclosed many amines as dyeing agents, including sterically hindered amines. On appeal, the Court held that the isolated presence in the prior art of a sterically hindered amine, outside the scope of the claims, failed to teach or suggest the significance of using the claimed class of sterically hindered amines. In re Langer, 465 F.2d 898-99, 175 USPQ at 171 (CCPA 1972). The presence of the Morris Ru compounds, which fall outside the scope of the present claims and which are neutrally charged and which complex the Ru metal via nitrogen atoms, fail to teach or suggest the significance of using the claimed Ru compounds.

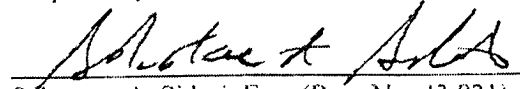
Accordingly, Applicants respectfully request that the 35 U.S.C. §103(a) rejection of claims 26 and 36 be withdrawn. Claims 27-35 and 37-45 ultimately depend from independent claims 26 and 36. If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 U.S.P.Q. 2d 1596 (Fed. Cir. 1988). Applicants therefore respectfully request that the rejection of claims 26-45 under 35 U.S.C. §103(a) as being obvious over Morris et al. and the Kuhlwein, Kramer, Everaere and Carmona references be withdrawn.

In view of the above amendments and remarks, Applicants respectfully request reconsideration of the application, withdrawal of the rejections under 35 U.S.C. §§102, 103, and 112, and request the issuance of a formal Notice of Allowance directed to claims claims 26-34, and 36-44. Should the Examiner have any questions about the above remarks, the undersigned attorneys would welcome a telephone call.

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Respectfully submitted,



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